# **Amendments To The Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

## In the Claims:

## What is claimed is:

Claims 1-12 (Cancelled)

- (New) A method of treating cancer in a mammal, comprising: administering to said mammal
  - (a) a compound of formula I

or a salt, solvate, or physiologically functional derivative thereof; wherein:

D is

$$X_2 - N$$
 $X_3$ 
 $X_2 - N$ 
 $X_3$ 
 $X_4$ 
 $X_4$ 
 $X_4$ 
 $X_4$ 
 $X_4$ 
 $X_5$ 
 $X_5$ 
 $X_5$ 
 $X_5$ 
 $X_7$ 
 $X_8$ 
 $X_8$ 

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X<sub>1</sub> is hydrogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, or C<sub>1-4</sub> hydroxyalkyl;

X<sub>2</sub> is hydrogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C(O)R<sup>1</sup>, or aralkyl;

X<sub>3</sub> is hydrogen or halogen;

 $X_4$  is hydrogen,  $C_{1^{\hspace{-0.05cm}-\hspace{-0.05cm}4}}$  alkyl,  $C_{1^{\hspace{-0.05cm}-\hspace{-0.05cm}4}}$  haloalkyl, heteroaralkyl, cyanoalkyl,

 $\hbox{-(CH$_2$)$}_pC \hbox{=CH$(CH$_2$)$}_tH, \hbox{-(CH$_2$)}_pC \hbox{=C(CH$_2$)$}_tH, \hbox{ or } C_{3^{-7}} \hbox{ cycloalkyl};$ 

p is 1, 2, or 3;

t is 0 or 1;

W is N or C-R, wherein R is hydrogen, halogen, or cyano;

 $Q_1$  is hydrogen, halogen,  $C_{1^{-2}}$  haloalkyl,  $C_{1^{-2}}$  alkyl,  $C_{1^{-2}}$  alkoxy, or  $C_{1^{-2}}$  haloalkoxy;  $Q_2$  is  $A^1$  or  $A^2$ :

 $Q_3$  is  $A^1$  when  $Q_2$  is  $A^2$  and  $Q_3$  is  $A^2$  when  $Q_2$  is  $A^1$ ;

wherein

 $A^1$  is hydrogen, halogen,  $C_{1\mbox{--}3}$  alkyl,  $C_{1\mbox{--}3}$  haloalkyl, -OR  $^1$  , and

 $A^2$  is the group defined by  $-(Z)_{m}-(Z^1)-(Z^2)$ , wherein

Z is CH2 and m is 0, 1, 2, or 3, or

Z is NR2 and m is 0 or 1, or

Z is oxygen and m is 0 or 1, or

Z is CH<sub>2</sub>NR<sup>2</sup> and m is 0 or 1:

Z1 is S(O)2, S(O), or C(O); and

 $Z^2$  is  $C_1.C_4$  alkyl,  $NR^3R^4$ , aryl, arylamino, aralkyl, aralkoxy, or heteroaryl:

R1 is C1-4 alkyl;

 $R^2$ ,  $R^3$ , and  $R^4$  are each independently selected from hydrogen,  $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl,  $-S(O)_2R^5$ , and  $-C(O)R^5$ ;

R5 is C1-4 alkyl, or C3-7 cycloalkyl; and

when Z is oxygen then Z1 is S(O)2 and when D is

then  $X_2$  is  $C_{1^{-4}}$  alkyl,  $C_{1^{-4}}$  haloalkyl,  $C(O)R^1$ , or aralkyl; and (b) a compound of formula II

or a salt, solvate, or physiologically functional derivative thereof; wherein

Y is CR<sup>6</sup> and V is N; or Y is CR<sup>6</sup> and V is CR<sup>7</sup>;

R<sup>5</sup> represents a group CH<sub>3</sub>SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyxy groups;

 $R^7$  is selected from the group consisting of hydrogen, halo, hydroxy,  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylamino and dif $C_{1-4}$  alkylamino:

U represents a phenyl, pyridyl, 3<u>H</u>-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1<u>H</u>-indazolyl, 2,3-dihydro-1<u>H</u>-indazolyl, 1<u>H</u>-benzimidazolyl, 2,3-dihydro-1<u>H</u>-benzimidazolyl or 1<u>H</u>-benzotriazolyl group, substituted by an R<sup>8</sup> group and optionally substituted by at least one independently selected R<sup>9</sup> group;

R<sup>8</sup> is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or  $\text{R}^8$  represents trihalomethylbenzyl or trihalomethylbenzyloxy; or  $\text{R}^8$  represents a group of formula

wherein each  $R^{10}$  is independently selected from halogen,  $C_{1-4}$  alkyl and  $C_{1-4}$  alkoxy; and n is 0 to 3; and

each  $R^9$  is independently hydroxy, halogen,  $C_{1\cdot4}$  alkyl,  $C_{2\cdot4}$  alkenyl,  $C_{2\cdot4}$  alkynyl,  $C_{1\cdot4}$  alkoxy, amino,  $C_{1\cdot4}$  alkylamino, di[ $C_{1\cdot4}$  alkyl]amino,  $C_{1\cdot4}$  alkylthio,  $C_{1\cdot4}$  alkylsulphinyl,  $C_{1\cdot4}$  alkylsulphonyl,  $C_{1\cdot4}$  alkylcarbonyl, carboxy, carbamoyl,  $C_{1\cdot4}$  alkoxycarbonyl,  $C_{1\cdot4}$  alkanoylamino, N-( $C_{1\cdot4}$  alkyl)carbamoyl, N-di(N-di(N-di)carbamoyl, N-di(N-di)carbamoyl, N-di(N-di

 (New) The method of claim 1, wherein (a) the compound of formula I is a compound of formula I<sup>a</sup>

or a salt, solvate or physiologically functional derivative thereof; wherein  $Q_3$  is  $A^1$  when  $Q_2$  is  $A^2$  and  $Q_3$  is  $A^2$  when  $Q_2$  is  $A^1$ ; wherein

 $\begin{array}{l} A^1 \text{ is hydrogen, halogen, } C_{1^{-3}} \text{ alkyl, and} \\ A^2 \text{ is the group defined by } -(Z)_m -(Z^1) -(Z^2), \text{ wherein} \\ Z \text{ is } CH_2 \text{ and m is } 0, 1, 2, \text{ or } 3; \\ Z^1 \text{ is } S(O)_2, S(0), \text{ or } C(O); \text{ and} \\ Z^2 \text{ is } C_{1^{-4}} \text{ alkyl, or } NR^3R^4; \end{array}$ 

 ${\sf R}^3$  and  ${\sf R}^4$  are each independently selected from hydrogen, or  ${\sf C}_{1^-\!4}$  alkyl; and

(b) the compound of formula II is a compound of formula IIa

or a salt, solvate or physiologically functional derivative thereof; wherein R<sup>11</sup> is –Cl or –Br, X is CH, N, or CF, and Z is thiazole or furan.

15. (New) The method of claim 1, wherein (a) the compound of formula I is a compound of formula I $^{\rm b}$ 

 $(1)^b$ 

or a salt, solvate, or physiological functional derivative thereof; and

(b) the compound of formula II is a compound of formula II<sup>b</sup>

or a salt, solvate, or physiological functional derivative thereof.

16. (New) The method of claim 1, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I b

; and

(b) the compound of formula II is a monohydrate ditosylate salt of a compound of formula II  $^{\rm b}$ 

17. (New) The method of claim 1, wherein the compound of formula I is a monohydrochloride salt of a compound of formula I <sup>b</sup>

; and

(b) the compound of formula II is an anhydrous ditosylate salt of a compound of formula II  $^{\rm b}$ 

- 18. (New) A pharmaceutical composition comprising:
  - (a) a compound of formula I

or a salt, solvate, or physiologically functional derivative thereof; wherein:

D is 
$$X_1$$
  $X_2$   $X_3$   $X_2$   $X_3$   $X_4$   $X_4$   $X_5$   $X_4$   $X_5$   $X_5$ 

X<sub>1</sub> is hydrogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, or C<sub>1-4</sub> hydroxyalkyl;

X<sub>2</sub> is hydrogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C(O)R<sup>1</sup>, or aralkyl;

X<sub>3</sub> is hydrogen or halogen;

 $X_4$  is hydrogen,  $C_{1^-4}$  alkyl,  $C_{1^-4}$  haloalkyl, heteroaralkyl, cyanoalkyl,

 $-(CH_2)_p C = CH(CH_2)_t H, \ -(CH_2)_p C = C(CH_2)_t H, \ or \ C_{3^{-7}} \ cycloalkyl;$ 

p is 1, 2, or 3;

t is 0 or 1;

W is N or C-R, wherein R is hydrogen, halogen, or cyano;

 $Q_1$  is hydrogen, halogen,  $C_{1^{-2}}$  haloalkyl,  $C_{1^{-2}}$  alkyl,  $C_{1^{-2}}$  alkoxy, or  $C_{1^{-2}}$  haloalkoxy;  $Q_2$  is  $A^1$  or  $A^2$ :

Q<sub>3</sub> is A<sup>1</sup> when Q<sub>2</sub> is A<sup>2</sup> and Q<sub>3</sub> is A<sup>2</sup> when Q<sub>2</sub> is A<sup>1</sup>;

wherein

A<sup>1</sup> is hydrogen, halogen, C<sub>1-3</sub> alkyl, C<sub>1-3</sub> haloalkyl, -OR<sup>1</sup>, and

 $A^2$  is the group defined by  $-(Z)_{m}-(Z^1)-(Z^2)$ , wherein

Z is  $CH_2$  and m is 0, 1, 2, or 3, or

Z is NR2 and m is 0 or 1, or

Z is oxygen and m is 0 or 1, or

Z is CH<sub>2</sub>NR<sup>2</sup> and m is 0 or 1;

 $Z^1$  is  $S(O)_2$ , S(O), or C(O); and

 $Z^2$  is  $C_{1-4}$  alkyl,  $NR^3R^4$ , aryl, arylamino, aralkyl, aralkoxy, or heteroaryl:

R1 is C1-4 alkyl;

 $R^2$ ,  $R^3$ , and  $R^4$  are each independently selected from hydrogen,  $C_{1\text{-}4}$  alkyl,  $C_{3\text{-}7}$  cycloalkyl,  $-S(O)_2R^5$ , and  $-C(O)R^5$ ;

R5 is C1.4 alkyl, or C3.7 cycloalkyl; and

when Z is oxygen then Z1 is S(O)2 and when D is

then  $X_2$  is  $C_{1^{-4}}$  alkyl,  $C_{1^{-4}}$  haloalkyl,  $C(O)R^1$ , or aralkyl; and (b) a compound of formula II

or a salt, solvate, or physiologically functional derivative thereof; wherein

Y is CR<sup>6</sup> and V is N;

or Y is CR6 and V is CR7:

R<sup>6</sup> represents a group CH<sub>3</sub>SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy groups;

 $R^7$  is selected from the group consisting of hydrogen, halo, hydroxy,  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylamino and di[ $C_{1-4}$  alkyl]amino;

U represents a phenyl, pyridyl, 3<u>H</u>-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1<u>H</u>-indazolyl, 2,3-dihydro-1<u>H</u>-indazolyl, 1<u>H</u>-benzimidazolyl, 2,3-dihydro-1<u>H</u>-benzimidazolyl or 1<u>H</u>-benzotriazolyl group, substituted by an R<sup>8</sup> group and optionally substituted by at least one independently selected R<sup>9</sup> group; R<sup>8</sup> is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl:

or R<sup>8</sup> represents trihalomethylbenzyl or trihalomethylbenzyloxy; or R<sup>8</sup> represents a group of formula

wherein each R<sup>10</sup> is independently selected from halogen, C<sub>1-4</sub> alkyl and C<sub>1-4</sub> alkoxy; and n is 0 to 3; and each R<sup>9</sup> is independently hydroxy, halogen, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> alkoxy, amino, C<sub>1-4</sub> alkylamino, di[C<sub>1-4</sub> alkyl]amino, C<sub>1-4</sub> alkylthio, C<sub>1-4</sub> alkylsulphinyl, C<sub>1-4</sub> alkylsulphonyl, C<sub>1-4</sub> alkylcarbonyl, carboxy, carbamoyl, C<sub>1-4</sub> alkoxycarbonyl, C<sub>1-4</sub> alkanoylamino, N-(C<sub>1-4</sub> alkyl)carbamoyl, N,N-di(C<sub>1-4</sub> alkyl)carbamoyl, cyano, nitro and trifluoromethyl.

19. (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a compound of formula I <sup>a</sup>

or a salt, solvate or physiologically functional derivative thereof;  $wherein \ Q_3 \ is \ A^1 \ when \ Q_2 \ is \ A^2 \ and \ Q_3 \ is \ A^2 \ when \ Q_2 \ is \ A^1;$  wherein

A<sup>1</sup> is hydrogen, halogen,  $C_{1^{-3}}$  alkyl, and A<sup>2</sup> is the group defined by  $-(Z)_m - (Z^1) - (Z^2)$ , wherein Z is CH<sub>2</sub> and m is 0, 1, 2, or 3; Z<sup>1</sup> is S(O)<sub>2</sub>, S(0), or C(O); and Z<sup>2</sup> is  $C_{1^{-4}}$  alkyl, or NR<sup>3</sup>R<sup>4</sup>.

 $\mbox{R}^{3}$  and  $\mbox{R}^{4}$  are each independently selected from hydrogen, or  $\mbox{C}_{1^{-4}}$  alkyl; and

(b) the compound of formula II is a compound of formula II a

$$H_3C \underset{O}{\overset{N}{\overset{}}{\overset{}}} \underset{N}{\overset{}{\overset{}}} \underset{N}{\overset{}} \underset{N}{\overset{}{\overset{}}} \underset{N}{\overset{}} \underset{N}{\overset{}}$$

or a salt, solvate or physiologically functional derivative thereof; wherein R<sup>11</sup> is –Cl or –Br, X is CH, N, or CF, and Z is thiazole or furan.

 (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula 1 is a compound of formula 1 b

or a salt, solvate, or physiological functional derivative thereof; and
(b) the compound of formula II is a compound of formula II b

(II) or a salt, solvate, or physiological functional derivative thereof.

 (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I<sup>b</sup>

; and

(b) the compound of formula II is a monohydrate ditosylate salt of the compound of formula II  $^{\rm b}$ 

 (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I b

; and

(b) the compound of formula II is an anhydrous ditosylate salt of the compound of formula II  $^{\rm b}$ 

23. (New) A pharmaceutical combination comprising: a compound of formula I, I<sup>a</sup> or I<sup>b</sup> or salt, solvate or physiologically functional derivative thereof, and a compound of formula II, II<sup>a</sup> or II<sup>b</sup> or salt, solvate or physiologically functional derivative thereof for use in therapy.

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24. (New) The use of a pharmaceutical combination comprising: a compound of formula I, I<sup>a</sup> or I<sup>b</sup> or salt, solvate or physiologically functional derivative thereof, and a compound of formula II, II<sup>a</sup> or II<sup>b</sup> or salt, solvate or physiologically functional derivative thereof for the preparation of a medicament useful in the treatment of cancer.